

1. A composition comprising a polypeptide conjugated to a *Streptococcus pneumoniae* capsular polysaccharide, wherein the polypeptide comprises a fragment of at least 400 contiguous amino acids of a *Streptococcus pneumoniae* pneumolysin protein, wherein the polypeptide lacks the amino acid sequence KVEND (SEQ ID NO:22), wherein
5 the polypeptide lacks hemolytic activity, and wherein the composition elicits an immune response against *Streptococcus pneumoniae* when administered to a mammal.

2. The composition of claim 1, wherein the *Streptococcus pneumoniae* pneumolysin protein comprises the amino acid sequence of SEQ ID NO:1.

3. The composition of claim 1, wherein the polypeptide comprises amino acids 1-460 of SEQ ID NO:1.

4. The composition of claim 1, wherein the polypeptide comprises amino acids 1-464
15 of SEQ ID NO:1.

5. The composition of claim 1, wherein the polypeptide comprises amino acids 1-465 of SEQ ID NO:1.

6. The composition of claim 1, wherein the polypeptide comprises amino acids 1-466
20 of SEQ ID NO:1.

7. The composition of claim 1, wherein the polypeptide comprises amino acids 1-469 of SEQ ID NO:1.

8. The composition of claim 1, wherein the polypeptide comprises amino acids 1-470
25 of SEQ ID NO:1.

9. The composition of claim 1, wherein the polypeptide lacks the amino acid
30 sequence EDKVEND (SEQ ID NO:23).

10. The composition of claim 1, wherein the polypeptide lacks the amino acid sequence YPQVEDKVEND (SEQ ID NO:24).

11. The composition of claim 1, wherein the polypeptide consists of amino acid residues 1-460 of SEQ ID NO:1.

12. The composition of claim 1, wherein the polypeptide consists of amino acid residues 1-464 of SEQ ID NO:1.

13. The composition of claim 1, wherein the polypeptide consists of amino acid residues 1-465 of SEQ ID NO:1.

14. The composition of claim 1, wherein the polypeptide consists of amino acid residues 1-466 of SEQ ID NO:1.

15. The composition of claim 1, wherein the polypeptide consists of amino acid residues 1-469 of SEQ ID NO:1.

16. The composition of claim 1, wherein the polypeptide consists of amino acid residues 1-470 of SEQ ID NO:1.

17. The composition of claim 1, wherein the capsular polysaccharide is selected from the group consisting of serotype 4, 6B, 9V, 14, 18C, 19F, and 23F.

18. The composition of claim 1, wherein the capsular polysaccharide is serotype 14.

19. The composition of claim 1, wherein the capsular polysaccharide is serotype 18C.

20. The composition of claim 1, wherein the composition comprises a plurality of different capsular polysaccharides selected from the group consisting of serotype 4, 6B, 9V, 14, 18C, 19F, and 23F.

5 21. The composition of claim 1, wherein the immune response comprises a humoral immune response.

22. The composition of claim 1, wherein the immune response comprises a cellular immune response.

10 23. The composition of claim 1, wherein the immune response is directed against a *Streptococcus pneumoniae* capsular polysaccharide.

15 24. The composition of claim 1, wherein the immune response is directed against a *Streptococcus pneumoniae* pneumolysin protein.

25 25. The composition of claim 1, wherein the immune response is directed against a *Streptococcus pneumoniae* capsular polysaccharide and a *Streptococcus pneumoniae* pneumolysin protein.

20 26. A mammalian expression vector comprising a promoter operably linked to a nucleotide sequence comprising a nucleic acid encoding a polypeptide comprising a fragment of at least 400 contiguous amino acids of a *Streptococcus pneumoniae* pneumolysin protein, wherein the polypeptide lacks the amino acid sequence KVEND (SEQ ID NO:22), wherein
25 the polypeptide lacks hemolytic activity, and wherein the polypeptide elicits an immune response against *Streptococcus pneumoniae* when the expression vector is administered to a mammal.

30 27. The mammalian expression vector of claim 26, wherein the *Streptococcus pneumoniae* pneumolysin protein comprises the amino acid sequence of SEQ ID NO:1.

28. The mammalian expression vector of claim 26, wherein the polypeptide comprises amino acids 1-460 of SEQ ID NO:1.

5 29. The mammalian expression vector of claim 26, wherein the polypeptide comprises amino acids 1-464 of SEQ ID NO:1.

30. The mammalian expression vector of claim 26, wherein the polypeptide comprises amino acids 1-465 of SEQ ID NO:1.

10 31. The mammalian expression vector of claim 26, wherein the polypeptide comprises amino acids 1-466 of SEQ ID NO:1.

32. The mammalian expression vector of claim 26, wherein the polypeptide comprises amino acids 1-469 of SEQ ID NO:1.

15 33. The mammalian expression vector of claim 26, wherein the polypeptide comprises amino acids 1-470 of SEQ ID NO:1.

20 34. The mammalian expression vector of claim 26, wherein the polypeptide lacks the amino acid sequence EDKVEND (SEQ ID NO:23).

35. The mammalian expression vector of claim 26, wherein the polypeptide lacks the amino acid sequence YPQVEDKVEND (SEQ ID NO:24).

25 36. The expression vector of claim 26, wherein the polypeptide consists of amino acid residues 1-460 of SEQ ID NO:1.

30 37. The mammalian expression vector of claim 26, wherein the polypeptide consists of amino acid residues 1-464 of SEQ ID NO:1.

38. The mammalian expression vector of claim 26, wherein the polypeptide consists of amino acid residues 1-465 of SEQ ID NO:1.

39. The mammalian expression vector of claim 26, wherein the polypeptide consists of amino acid residues 1-466 of SEQ ID NO:1.

40. The mammalian expression vector of claim 26, wherein the polypeptide consists of amino acid residues 1-469 of SEQ ID NO:1.

41. The mammalian expression vector of claim 26, wherein the polypeptide consists of amino acid residues 1-470 of SEQ ID NO:1.

42. The mammalian expression vector of claim 26, wherein the immune response comprises a humoral immune response.

43. The mammalian expression vector of claim 26, wherein the immune response comprises a cellular immune response.

44. The mammalian expression vector of claim 26, wherein the immune response is directed against a *Streptococcus pneumoniae* pneumolysin protein

45. A mammalian expression vector comprising a promoter operably linked to a nucleotide sequence comprising a nucleic acid encoding a *Streptococcus pneumoniae* autolysin polypeptide, wherein the polypeptide elicits an immune response against *Streptococcus pneumoniae* when the expression vector is administered to a mammal.

46. The mammalian expression vector of claim 45, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:14.

47. The mammalian expression vector of claim 45, wherein the polypeptide consists of the amino acid sequence of SEQ ID NO:14.

48. The mammalian expression vector of claim 45, wherein the immune response comprises a humoral immune response.

5 49. The mammalian expression vector of claim 45, wherein the immune response comprises a cellular immune response.

50. A mammalian expression vector comprising a promoter operably linked to a nucleotide sequence comprising a nucleic acid encoding a *Streptococcus pneumoniae* pneumococcal surface protein A polypeptide, wherein the polypeptide elicits an immune response against *Streptococcus pneumoniae* when the expression vector is administered to a mammal.

10 51. The mammalian expression vector of claim 50, wherein the polypeptide comprises the amino acid sequence of SEQ ID NO:18.

52. The mammalian expression vector of claim 50, wherein the polypeptide consists of the amino acid sequence of SEQ ID NO:18.

20 53. The mammalian expression vector of claim 50, wherein the immune response comprises a humoral immune response.

54. The mammalian expression vector of claim 50, wherein the immune response comprises a cellular immune response.

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55. A polypeptide consisting of an amino acid sequence selected from the group consisting of amino acids 1-460 of SEQ ID NO:1, amino acids 1-464 of SEQ ID NO:1, amino acids 1-466 of SEQ ID NO:1, and amino acids 1-469 of SEQ ID NO:1.

56. A method of inducing an immune response in a mammal, the method comprising administering to a mammal an amount of the composition of claim 1 effective to induce an immune response against *Streptococcus pneumoniae* in the mammal.

5 57. The method of claim 56, wherein the immune response is a prophylactic immune response.

58. The method of claim 56, wherein the immune response is a therapeutic immune response.

10 59. The method of claim 56, wherein the immune response is cross-reactive against at least one *Streptococcus pneumoniae* serotype that differs from the serotype of the capsular polysaccharide present in the composition.

15 60. The method of claim 59, wherein the capsular polysaccharide is serotype 7.

61. The method of claim 59, wherein the capsular polysaccharide is serotype 6B.

62. The method of claim 59, wherein the capsular polysaccharide is serotype 18C.

20 63. The method of claim 59, wherein the capsular polysaccharide is serotype 23F.

64. The method of claim 56, wherein the immune response is cross-reactive against at least one non-*Streptococcus pneumoniae* member of the *Streptococcus* genus.

25 65. A method of inducing an immune response in a mammal, the method comprising administering to a mammal an amount of the expression vector of claim 26 effective to induce an immune response against *Streptococcus pneumoniae* in the mammal.

30 66. The method of claim 65, wherein the immune response is cross-reactive against at least one non-*Streptococcus pneumoniae* member of the *Streptococcus* genus.

67. A method of inducing an immune response in a mammal, the method comprising administering to a mammal an amount of the expression vector of claim 45 effective to induce an immune response against *Streptococcus pneumoniae* in the mammal.

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68. The method of claim 67, wherein the immune response is cross-reactive against at least one non-*Streptococcus pneumoniae* member of the *Streptococcus* genus.

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69. A method of inducing an immune response in a mammal, the method comprising administering to a mammal an amount of the expression vector of claim 50 effective to induce an immune response against *Streptococcus pneumoniae* in the mammal.

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70. The method of claim 69, wherein the immune response is cross-reactive against at least one non-*Streptococcus pneumoniae* member of the *Streptococcus* genus.

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71. A method of inducing an immune response in a mammal, the method comprising:
administering to a mammal a mammalian expression vector comprising a promoter operably linked to a nucleotide sequence comprising a nucleic acid encoding a *Streptococcus pneumoniae* pneumolysin polypeptide or antigenic fragment thereof; and
administering to the mammal a purified pneumolysin polypeptide or antigenic fragment thereof,
wherein the combined administrations elicit an immune response against *Streptococcus pneumoniae* pneumolysin in the mammal.

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72. The method of claim 71, wherein the mammal is administered at least two separate doses of the expression vector.

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73. The method of claim 71, wherein the administration of the pneumolysin polypeptide or antigenic fragment thereof is at least one week after the administration of the expression vector.

74. A composition comprising a polypeptide conjugated to a non-*Streptococcus pneumoniae* bacterial polysaccharide, wherein the polypeptide comprises a fragment of at least 400 contiguous amino acids of a *Streptococcus pneumoniae* pneumolysin protein, wherein the polypeptide lacks the amino acid sequence KVEND (SEQ ID NO:22), wherein
 5 the polypeptide lacks hemolytic activity, and wherein the composition elicits an immune response against the non-*Streptococcus pneumoniae* bacterium when administered to a mammal.

75. The composition of claim 74, wherein the non-*Streptococcus pneumoniae*
 10 bacterium is selected from the group consisting of pneumococcus, haemophilus influenza type b, meningococcal group A, B or C, and group B streptococcus type Ia, Ib, II, III, V or VIII.

76. A method of inducing an immune response in a mammal, the method comprising
 15 administering to a mammal an amount of the composition of claim 74 effective to induce an immune response against the non-*Streptococcus pneumoniae* bacterium in the mammal.

77. The method of claim 76, wherein the non-*Streptococcus pneumoniae* bacterium
 20 is selected from the group consisting of pneumococcus, haemophilus influenza type b, meningococcal group A, B or C, and group B streptococcus type Ia, Ib, II, III, V or VIII.

78. A purified antibody that binds to the composition of claim 1.

79. A method of treating or preventing *Streptococcus pneumoniae* infection in a
 25 mammal, the method comprising administering to a mammal a therapeutically or prophylactically effective amount of a purified antibody that binds to the composition of claim 1.